Archives of Razi Institute, Vol. 76, No. 4 (2021) 965-974

DOI: 10.22092/ari.2021.356007.1763

Original Article

Effect of Electroactive Water Solutions on Homeostasis and Healing Processes of Intestinal Anastomosis Combined with Simulated Anemia in Wistar Rats

Gorelik, S. G[1*], Kolesnikov, S. A[1], Zheludev, A. A[2], Parkhisenko, Y. A[2], Bulynin, V. V[2]

1. Belgorod State University, 85, Pobedy St., Belgorod, 308015, Russia
2. Voronezh State Medical University named after N.N. Burdenko, 10, Studencheskaya st., Voronezh, 394036, Russia

Received 11 September 2021; Accepted 27 September 2021
Corresponding Author: gorelik@bsu.edu.ru

Abstract

Gastroduodenal bleeding is one of the most challenging issues in surgery nowadays. The crude mortality rate due to severe blood loss in gastrointestinal bleeding is very high. Therefore, the use of medications to prevent severe blood loss and protect cells from the harmful effects of hypoxia should be the focus of attention in these conditions. This experimental study was carried out to establish changes in blood parameters and humoral immunity in rats after intestinal anastomoses combined with acute blood loss after the application of catholyte and anolyte. The study included 45 male Wistar rats weighing 290-320 g that were divided equally (15 animals per group) into three groups of intact animals (group 1), animals exposed to the small bowel resection (1.5 cm) with the end-to-end anastomosis and simulated acute blood loss (group 2), and animals exposed to the small bowel resection with end-to-end anastomosis and simulated acute blood loss that were daily given catholyte in the postoperative period group (group 3). After the surgery, the rats were given a catholyte solution *per os*, and the operative wound was treated with an anolyte. The blood samples and the wall of the small intestine in the anastomotic zone were used as a biological substrate to study the effect of catholyte on changes in the body during the healing process. The experiment was conducted for 15 days, and the data were recorded in two intervals on the 5^{th} and 15^{th} days after starting the experiment. The analyzed materials evidenced that the use of catholyte and liquid with negative oxidoreduction potential (ORP) (minus 500-520 mV) resulted in positive changes in the blood cell count, humoral immunity, and phagocytic activity impaired after the small bowel resection and blood loss. The use of an anolyte disinfectant (liquid with positive ORP+710-770 mV) prevented bacterial contamination of the surgical wound. The obtained findings proved that the catholyte had a positive effect on humoral immunity and healing processes in the anastomotic zone. Furthermore, the anolyte prevented the development of purulent complications and inflammation in the area of the surgical wound, and therefore, promoted the healing processes.

Keywords: Anolyte, Catholyte, Immunity, Intestinal anastomosis, Oxidoreduction potential (ORP)

1. Introduction

Gastroduodenal bleeding is one of the most challenging issues in surgery nowadays. Upper gastrointestinal (GI) bleeding occurs annually in 50-170 people per 100,000 population (1, 2). The crude mortality rate due to severe blood loss in GI bleeding is very high and constitutes 11.3% (3, 4). Therefore, the use of medications to prevent severe blood loss and protect the cells from the harmful effects of hypoxia should be the focus of attention in these conditions (5, 6).

In the early hours after a traumatic injury or surgery, metabolism is associated with a reduction in the body's overall energy expenditure and nitrogen loss. As soon as the patient is properly resuscitated and stabilized, the re-use of the substrate will be necessary to maintain the function of vital organs and repair damaged tissues. This step is known by maintaining homeostasis companies, such as the rate of metabolism of the added oxygen and preferred enzyme substrates for the oxidation of glucose and stimulation of the immune system to identify alternative continuous metabolism of amino acids (proteins), carbohydrates, and lipids in patients. They build on the premise that metabolic and nutritional support is limited (2, 7, 8).

Feeding is usually done through a gastric tube; however, in some cases, surgical replacement of the jejunostomy tube is more appropriate, especially when less aggressive fans are useful (9, 10). A wide range of diseases affects the colon, such as benign and malignant neoplasms (11, 12), inflammatory bowel disease (11, 13), and others that are often treated with resection and anastomosis of the colon (14). Oral nutrition is safe after elective colorectal surgery and can be tolerated by most patients; therefore, it may be a routine procedure in the postoperative treatment of such patients (15, 16).

Adequate nutrition is a major goal in postoperative treatment; however, the presence of ileus after abdominal surgery is a major obstacle that gastric catheter is used to deal with and reduces ileus (17). Recently, many studies have shown that the routine use of a gastric catheter in abdominal and colorectal surgeries is not necessary (18-20).

Electroactive aqueous solutions have a wide range of biological properties. They have low toxicity for enteral and parenteral administration. It has been established that the catholyte has an anabolic effect and stimulates growth processes, as well as physiological and reparative regeneration (21, 22). One of the well-studied effects of anolyte is antiseptic action. It is absolutely safe for living organisms (4, 23, 24). Due to these properties, electroactive aqueous solutions are increasingly used in medical practice. The use of electroactive aqueous solutions in the postoperative period under acute GI bleeding has not been previously studied (4, 23-25). The current study aimed to investigate the effect of electroactive aqueous solutions on homeostasis and healing processes under the small bowel resection combined with simulated blood loss and anemia.

2. Material and Methods

2.1. Animal and Experimental Conditions

All chemicals were purchased from Sigma Aldrich unless otherwise stated. In total, 45 adult male Wistar rats weighing 250-300 g were used in this study as the animal model to conduct the whole experiment. The animals were housed under controlled environmental conditions (20±2°C, 12:12h light: dark cycle) and allowed ad libitum access to food and water. All the animals were divided into three groups of 15 rats per group, namely group 1 (intact animals that were not exposed to any interventions), group 2 (controls that underwent intestinal anastomosis with simulated acute blood loss), and group 3 (cases that underwent intestinal anastomosis with simulated acute blood loss and received catholyte).

2.2. Experimental Procedure

In this study, the chest of the animals was opened under deep anesthesia. The animals were anesthetized by an injection of 0.10 ml of ketamine (15 mg/kg b.w.): xylazine (10 mg/kg b.w.) mixture into the peritoneal cavity. Blood was aspirated from the rat heart with a sterile syringe, and 5 mL of blood was taken for biochemical, clinical, and immunological studies. Blood serum analyses were carried out in the Central Scientific Research Laboratory of Voronezh N.N. Burdenko State Medical University using a biochemical semi-automatic analyzer Stat Fax 1904 (USA) and DiaSys reagent kits (Germany) (26).

Acute blood loss was simulated a day before surgery. Rats were injected intraperitoneally with 100 IU heparin, and 5-10 min after that procedure, the tip of the tail was cut off. Blood was collected in a graduate glass to assess the volume of blood loss. Hemoglobin levels were monitored using a Sahli's hemoglobinometer.

The anterior abdominal wall was shaved prior to surgery. Ceftriaxone 2 mg/kg was injected subcutaneously, and zoletil was administered intraperitoneally 40 mg/kg for anesthesia. The anterior abdominal wall was treated twice with anolyte (Oxidoreduction potential+700-900 mV). A median laparotomy was performed, and a loop of the small intestine was pulled out. Subsequently, the small intestine was resected for 1.5 cm, after which an end-to-end intestinal anastomosis was formed with a two-row Albert stitch. The first row of sutures was applied with 7/0 Vicryl, and the second row of sutures was applied with 7/0 polypropylene. After applying anastomosis, the abdominal wall was sutured with continuous twisting peritoneal-aponeurotic and then skin sutures. The peritoneum and the surgery area were treated with anolyte.

The biological material samples (blood and the wall of the small intestine) were taken on the 5th and 15th days after starting the experiment. The venous blood was taken for investigation in tubes "Vacuette" and "Greiner bio-one" (Austria) to obtain serum and citrated plasma.

This morphological study aimed to investigate quantitative and qualitative changes in the cellular composition in animals after the anastomosis formation on the proposed methods for the prevention of insolvency and to assess the effect of electroactive aqueous solutions on the healing processes in anastomoses (Figure 1). After defatting and making sections, the specimens were stained with hematoxylin and eosin and examined under a light microscope at various magnifications. For this purpose, the cellular composition of the studied organ was determined in 10 fields of view using an eyepiece-manometer MOV-1 according to G.G. Avtandilov's technique. After that, the presence and prevalence of inflammatory changes in the anastomotic area were visually assessed. The investigation was performed on the day of the biomaterial sampling. Catholyte was used *per os*, as a beverage, daily during the entire observation period instead of drinking water.

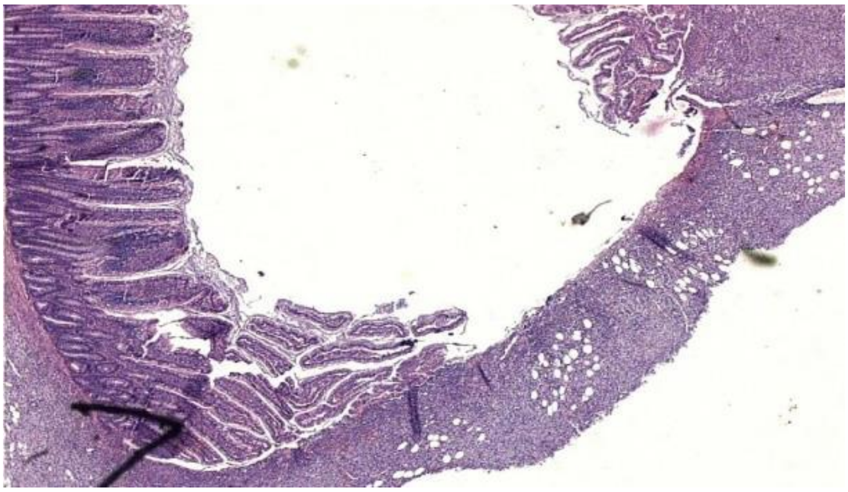

Figure 1. Cytological picture of the wound discharge of the intestine on the 5th day in the spontaneous healing process (Staining according to Romanovsky-Giemsa, Magnification 100×)

2.3. Statistical Analysis

The recorded data were analyzed in SPSS software (version 10; SPSS Inc., Chicago, Illinois, USA) through the Pearson chi-square test and Student's t-test.

3. Results and Discussion

The therapeutic effect on the inflammatory processes in the body and anastomotic zones were assessed based on the results of a complete blood count (CBC), investigations of the phagocytic activity, and the level of immunoglobulins as previously described by (1, 3, 26). Table 1 demonstrates the results of a CBC in animals of all groups.

Table 1. Dynamics of the complete blood count parameters (M±m, n=45) under acute blood loss in the postoperative period

Parameter	Group 1 (n=15)	Group 2 (n=15)		Group 3 (n=15)	
		On the 5th day	On the 15th day	On the 5th day	On the 15th day
Erythrocytes, 10*12/l	5.95±0.41	4.09±0.24*	5.1±0.73	5.35±0.2#	5.59±0.85
Hemoglobin, g/l	124.4±7.05	85.5±3.6*	107.67±3.5*	116.5±4.2#	132.8±9.8#
Platelets, 10*9/l	542±57.2	350±41.2*	427.3±94.6	436.8±77.7#	561.8±50.5
Leukocytes, 10*9/l	10.4±1.94	7.7±0.7	10.8±0.7	9.12±1.08	9.94±0.2
Stabs, %	1.125±0.58	1.6±0.6	3±0.7*	1.2±0.3	1.6±0.5#
Segmented, %	29.5±4.9	10.3±2.4*	18.3±3.6*	17.2±3.8*#	21.2±4.03
Monocytes, %	1.5±1.05	7.3±2.4*	5.2±0.6*	10±1.4*	10.8±1.6*#
Lymphocytes, %	67.75±2.86	79.7±4.3*	68.8±2.3	67.7±4.5#	70.2±5.1
ESR, mm/h	1.25±0.49	4.6±1.65*	1.6±0.7	2.5±0.8#	7.4±2.1*#

* P<0.05 compared to the animals in group 1
\# P<0.05 compared to the animals in group 2

On the 5th day after the surgery, the level of erythrocytes decreased by 1.5 times without the use of catholyte in the animals in group 2. On the 15th day after the surgery, the level of erythrocytes in the animals in group 3 increased by 1.3, compared to the animals in group 2. In addition, on the 5th day, the hemoglobin level decreased by 31.3%, compared to the animals in group 1, and on the 15th day, the hemoglobin level decreased by 13.4%, compared to the animals in group 1. These results were in line with the findings of the previously published studies (4, 6). With the catholyte application on the 5th day after the surgery, the hemoglobin level increased by 36% in the animals in group 3, compared to the animals in group 2, and on the 15th day after the surgery, the hemoglobin level also increased by 23.5% in the animals in group 3, compared to the animals in group 2.

The observed changes in erythrocytes and hemoglobin reliably evidence the stimulating effect of the cationic solution on erythropoiesis in rats in the presence of anemia and the resulted normalization of hemoglobin (2, 9, 27). On the 5th day after the surgery, the platelet level in the animals in group 2 decreased by 1.5 times. With the catholyte application, on the 5th day following the surgery, the platelet level in the animals in group 3 increased by 1.2 times, compared to the animals in group 2. In this study, the dynamics of platelet changes by groups correlates with the blood loss amount, which is consistent with the findings of previously published studies (17) although the stimulating effect of the cationic solution in animals in the experimental group is not excluded on the 15th day.

In group 2, the level of stabs increased by 1.9 times, compared to the animals in group 1. With the catholyte application, the level of stabs decreased by 1.9 times in the animals in group 3. In the animals in group 2, the level of segmented leukocytes decreased by 2.9 times, compared to the animals in group 1, and on the 5th day following the surgery, the level of segmented leukocytes in the animals in group 2 decreased by 1.6 times similar to the findings of the previously published studies (17, 24, 25). With the catholyte application, on the 5th day after the surgery, the level of segmented leukocytes in the animals in group 2 decreased by 1.7 times, compared to the animals in group 1. With the catholyte application, on the 5th day following the surgery, the level of segmented leukocytes in the animals in group 3 increased by 1.7 times, compared to the animals in group 2.

Changes in leukocytes in the control and experimental groups also correlate with the blood loss amount and prove the absence of significant inflammatory changes (24). The increased level of stab leukocytes by 5 or more in the animals in group 2 on the 15th day after the surgery also evidences the anti-inflammatory effect of the catholyte solution in the animals in the experimental group (24, 25).

The level of monocytes in the animals in group 2 increased by 5 times on the 5th day following the surgery and 3.5 times on the 15th day after the surgery, compared to the animals in group 1. With the catholyte application, the level of monocytes in the animals in group 3 increased by 6.7 times on the 5th day after the surgery, as well as 7 and 2 times on the 15th day after the surgery, compared to the animals in group 2. A significant increase in monocytes among the animals in group 2, especially in the animals in group 3, compared to the controls during the phase of wound inflammation and the regeneration phase reflects the need for phagocytosis and bactericidal activity (24, 25).

On the 5th day following the surgery, the level of lymphocytes in the animals in group 2 increased by 18%, compared to the animals in group 1. Furthermore, on the 5th day following the surgery, the level of lymphocytes in the animals in group 3 decreased by 14.5%, compared to the animals in group 2. Moreover, on the 5th day following the surgery, the erythrocyte sedimentation rate (ESR) level in the animals in group 3 decreased by 1.8 times, compared to the animals in group 2. On the 15th day after the surgery, it increased by 4.6 times, compared to the animals in group 2 similar to the findings of a study conducted by Lau, Yu (25).

Changes in the lymphocyte level are more evident in the control group on the 5th days after the surgery and are less pronounced on the 15th day following the surgery, which is likely to reflect the intensity of lymphocytic activity (their subpopulations). This lymphocytic tension is not detected in the group where catholyte solutions were applied. On the 5th day following the surgery, the ESR level in the animals in group 2 increased by 3.7 times, compared to the animals in group 1, and on the 15th day after the surgery, the ESR level in the animals in group 3 increased by 6 times, compared to the animals in group 1. Blood loss and aseptic inflammation in the area of the anastomosis and the surgical wound result in an increased ESR level as discussed by Lau, Yu (25).

The use of cationic solutions provides an increase in ESR on the 5th day following the surgery, compared to the animals in the control group and even more on the 15th day after the surgery that can probably be attributed to an increase in the cationic reaction of immunoglobulins and the protein composition of the blood plasma.

The phagocytic activity in the animals in group 2 decreased by 2 times on the 15th day after the surgery, compared to the animals in group 1 (Table 2). The phagocytic activity in the animals in group 3 decreased by 4.3 times on the 15th day after the surgery. On the 15th day after the surgery, the phagocytic activity in the animals in group 3 was 1.4 times less, compared to the animals in group 2. Furthermore, on the 15th day after the surgery, the phagocytic index in the animals in group 2 decreased 2.1 times, compared to the animals in group 1, and the phagocytic index in the animals in group 3 decreased by 281 times, compared to the animals in group 2.

Accordingly, the study of the phagocytic activity and the phagocytic index in different experimental groups showed a decrease in their parameters confirming secondary immunodeficiency states, which is less pronounced in the group where catholyte was applied. Therefore, the study of the phagocytic activity and the phagocytic index demonstrated a decrease in the parameters of the animals of the comparison groups, which reflected changes in inflammatory conditions and immunodeficiency states; however, they were less pronounced in the group where the catholyte was used.

The content of IgG in the blood serum, as a rule, increased with chronic or recurrent infections that pronounced inflammatory processes (4). After the small bowel resection and enteroanastomosis combined with blood loss, the level of Jg G increased by 3.4 times on the 5th day after the surgery and by 2.6 times on the 15th day after the surgery, compared to the animals in group 1. With the use of catholyte, the level of IgG in the animals in group 3 decreased by 1.2 times on the 5th day after the surgery and decreased by 1.4 times on the 15th day after the surgery, compared to the animals in group 2. Due to catholyte application, the level of IgG in the animals in group 3 remains higher than that in the animals in group 1; however, it was lower in animals in group 2 and showed a fact that proved decreased inflammatory reactions in the animals (Table 3).

Table 2. Dynamics of the phagocytic activity parameters (M±m, n=45) during drug correction of intestinal anastomosis healing

Group 1 (n=15)		**Group 2 (n=15)**		**Group 3 (n=15)**	
		On the 5th day	On the 15th day	On the 5th day	On the 15th day
Phagocytic activity	58.9±10.6	49±3.8	29.3±6.6*	45.3±7.3	13.8±2.8*#
Phagocytic index	8.1±1.8	7.6±1.9	3.85±0.49*	5.4±0.9	2.86±0.7*

* $P<0.05$ compared to the animals in group 1
\# $P<0.05$ compared to the animals in group 2

Table 3. Dynamics of the humoral immunity parameters (M±m, n=45) during drug correction of intestinal anastomosis healing

Parameters, mg/dL	**Group 1 (n=15)**	**Group 2 (n=15)**		**Group 3 (n=15)**	
		On the 5th day	**On the 15th day**	**On the 5th day**	**On the 15th day**
IgG	40.18±0.79	98.3±0.73*	143.3±14.3*	84±2.5*#	103.3±5.1*#
IgA	13.49±0.47	24±0.25*	8.67±2.87*	46.3±5.2*#	23±3.8*#
IgM	3.24±0.12	11±0.76*	9.67±1.43*	16±2.5*#	15.7±1.4*#

* $P<0.05$ compared to the animals in group 1
\# $P<0.05$ compared to the animals in group 2

IgA is an important factor of local immune protection at the level of the mucous membrane of the GI tract (2, 27). Significant variations of this parameter were observed in the animals in group 2. On the 5th day after the surgery, there was a significant increase by 1.7 times, compared to the initial findings, which reflected the stressed state of IgA due to blood loss and surgical interventions.

On the 15th day after the surgery, there was a pronounced deficit of IgA by 0.6 times. With the use of catholyte, there was an increase in IgA by 3.4 times on the 5th day after the surgery, and it remained 1.9 higher in the animals in group 1 on the 15th day after the surgery. This fact evidences the stimulating effect of catholyte on the synthesis of IgA. IgM provides humoral immunity and primary immune response. In our studies, its level increased by 3.4 times in the animals in group 2 on the 5th day after the surgery, compared to the initial findings (group 1), and by 3 times on the 15th day after the surgery that proved the stability of humoral immunity during these periods despite the blood loss.

The use of catholyte in the animals in group 3 significantly increased the level of IgM by 4.9 times on the 5th day after the surgery and 4.8 times on the 15th day after the surgery, compared to the initial level. At the same time, the level of IgM increased by 1.5 times on the 5th day after the surgery and 1.6 times on the 15th day after the surgery, compared to the animals in group 2. Therefore, the use of catholyte promotes the synthesis of Ig M by B-lymphocytes and provides a high level of natural immunity, as well as anti-infectious protection.

A surgical intervention associated with blood loss is characterized by significant violations of the blood system and immunity. The use of catholyte, being a powerful antioxidant and stimulator of regenerative processes, allowed preventing the deterioration of the state of homeostasis and eliminating the violations of some parameters of the immune process.

On the 15th day after the formation of the anastomosis, necrosis and hemorrhages were observed in the animals in the control group, and at the same time, fibrin and epithelial cells were detected in tissue detritus (Figure 2). Around the anastomosis, the zone of demarcation inflammation was manifested by the plethora of blood vessels at the microcirculatory level in varying degrees of severity by a cellular reaction.

Inflammatory-necrotic changes were observed with the signs of epithelialization of the defect along the edge in the intestinal wall in the animals in the control group on the 15th day after surgery in the anastomotic area (Staining according to Van Gieson; Figure 3).

On the 15th day after surgery, the inflammatory response significantly decreased, and the wound surface was covered with newly formed epithelium. The vessels of the granulation tissue became vertically oriented, and there was a horizontal orientation of fibroblasts and the formation of bundles of mature collagen fibers. Therefore, there was an inflammatory process in the muscular and serous membranes with lymphocytic infiltration. The serous membrane was lined with a single-layer squamous epithelium, and the fields of connective tissue were moderately expressed. Accordingly, the dynamics of the inflammatory process were evident.

In the group of animals where catholyte was used, on the 5th day after surgery, there were fibrocytes and cicatricial changes; moreover, the wound was epithelized, and there was a growth of the glandular epithelium from the edges of the wounds and no granulation tissue.

On the 15th day after surgery, inflammation persisted in the group of animals where catholyte was used (Figure 4). The wound was epithelialized, and residual inflammation was replaced by the connective tissue; moreover, the sutures were visible in the scar, and the intestine was epithelialized.

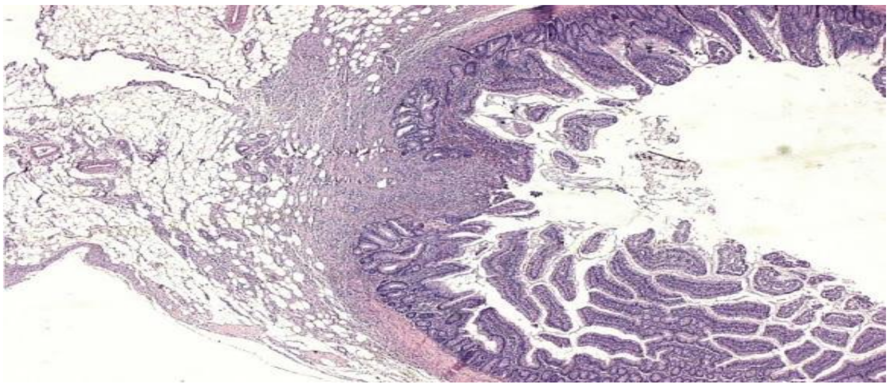

Figure 2. Cytological picture of the intestinal anastomosis on the 15th day after surgery (Staining according to Romanovsky-Giemsa, Magnification 100×)

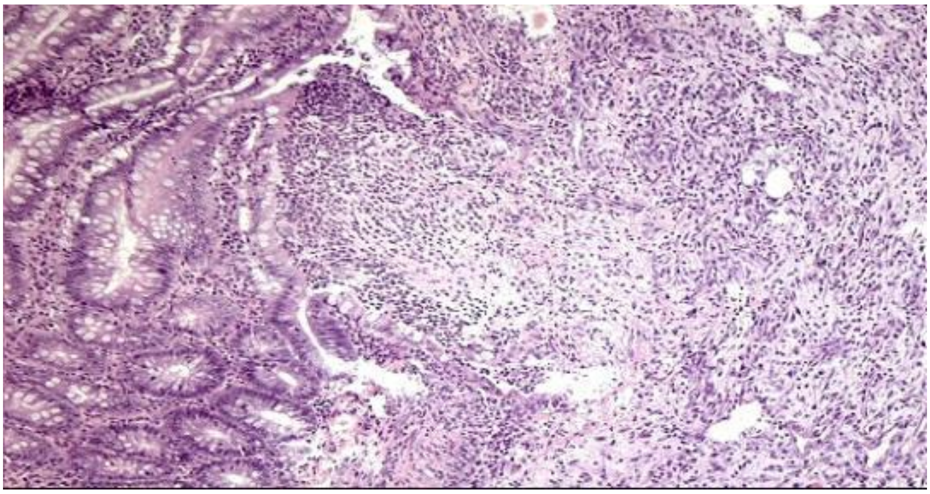

Figure 3. Cytological picture of the intestinal wall on the 5th day after surgery and the use of catholyte (Staining according to Van Gieson, Magnification 200×)

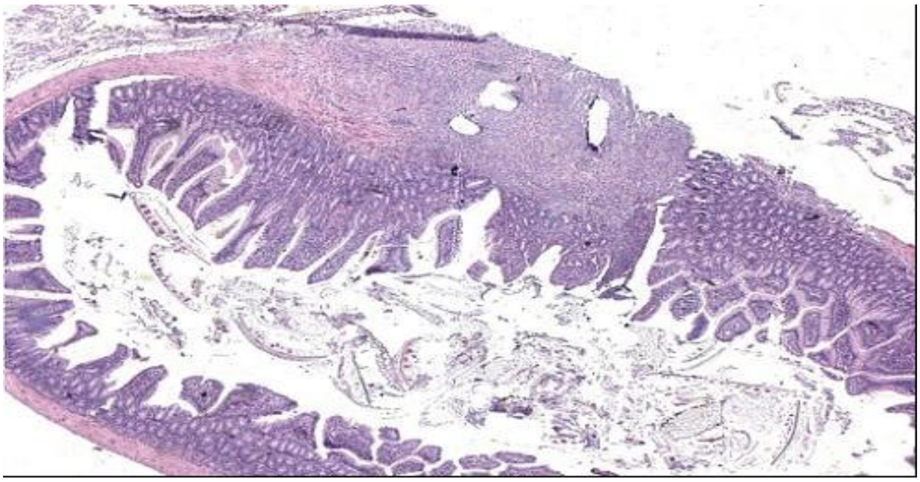

Figure 4. Cytological picture of the intestinal wall on the 15th day after surgery and the use of catholyte (Staining according to Van Gieson, Magnification 100×)

4. Conclusion

In conclusion, anastomosis combined with simulated blood loss and anemia was formed and healed much worse in the presence of pronounced changes in phagocytic activity, erythropoiesis, and humoral immunity. Moreover, the use of catholyte in the experimental group demonstrated an immunostimulating and immunostabilizing action that ensured the stability of the humoral immunity. Furthermore, anolyte, being a powerful antiseptic, prevented inflammation and suppuration in the area of the postoperative scar, and therefore, promoted the healing of the intestinal anastomosis.

Authors' Contribution

Study concept and design: S. G. G.
Acquisition of data: S. A. K.
Analysis and interpretation of data: A. A. Z.
Drafting of the manuscript: Y. A. P.
Critical revision of the manuscript for important intellectual content: S. G. G. and A. A. Z.
Statistical analysis: V. V. B.

Administrative, technical, and material support: Y. A. P.

Ethics

Experimental animals were managed and treated in compliance with the requirements of Order No.1045-73 "Sanitary rules for the arrangement, equipment, and maintenance of vivarium (s)" dated April 6, 1973, the Ministry of Health of the USSR, Order No. 1179 dated October 10, 1983, the Ministry of Health of the USSR, Order No. 267 dated June 19, 2003, the Ministry of Health of the Russian Federation; of the "Rules for the handling, maintenance, anesthesia, and killing of experimental animals", approved by the Ministry of Health of the USSR (1977) and the Ministry of Health of the RSFSR (1977). Moreover, the principles of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1986) and the WMA Declaration of Helsinki on the humane treatment of animals (1996) were observed in this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Ikizler TA, Cano NJ, Franch H, Fouque D, Himmelfarb J, Kalantar-Zadeh K, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. Kidney Int. 2013;84(6):1096-107.
2. Scott M, Baldini G, Fearon K, Feldheiser A, Feldman L, Gan T, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 1: pathophysiological considerations. Acta Anaesthesiol Scand. 2015;59(10):1212-31.
3. Aider M, Gnatko E, Benali M, Plutakhin G, Kastyuchik A. Electro-activated aqueous solutions: theory and application in the food industry and biotechnology. Innov Food Sci Emerg Technol. 2012;15:38-49.
4. Кошелев П, Глухов А, Расчепеев Д, Остроушко A. Method of Treatment Posttraumatic Synovitis Using Aqueous Anolyte and Catholyte. J Exp Clin Surg. 2015;8(4):364-8.
5. Wilcoxon F. Individual comparisons by ranking methods. Breakthroughs in statistics: Springer; 1992. p. 196-202.
6. Yang Y-X, Lewis JD, editors. Prevention and treatment of stress ulcers in critically ill patients. Semin Gastrointest Dis; 2003;14(1):11-9.
7. Gordy S, Kozar RA. Metabolism in the Trauma Patient. Surgical Metabolism: Springer; 2014. p. 97-109.
8. Mahdy T, Schou C. Efficacy of single anastomosis sleeve ileal (SASI) bypass for type-2 diabetic morbid obese patients: Gastric bipartition, a novel metabolic surgery procedure: A retrospective cohort study. Int J Surg. 2016;34:28-34.
9. Koivusalo AI, Sistonen SJ, Lindahl HG, Rintala RJ, Pakarinen MP. Long-term outcomes of oesophageal atresia without or with proximal tracheooesophageal fistula–gross types A and B. J Pediatr Surg. 2017;52(10):1571-5.
10. Lázár G, Kaszaki J, Ábrahám S, Horváth G, Wolfárd A, Szentpáli K, et al. Thoracic epidural anesthesia improves the gastric microcirculation during experimental gastric tube formation. Surgery. 2003;134(5):799-805.
11. King JA, Underwood FE, Panaccione N, Quan J, Windsor JW, Kotze PG, et al. Trends in hospitalisation rates for inflammatory bowel disease in western versus newly industrialised countries: a population-based study of countries in the Organisation for Economic Co-operation and Development. Lancet Gastroenterol Hepatol. 2019;4(4):287-95.
12. Levy AD, Murakata LA, Abbott RM, Rohrmann Jr CA. From the archives of the AFIP: benign tumors and tumorlike lesions of the gallbladder and extrahepatic bile ducts: radiologic-pathologic correlation. Radiographics. 2002;22(2):387-413.
13. Vuksic T, Zoricic I, Brcic L, Sever M, Klicek R, Radic B, et al. Stable gastric pentadecapeptide BPC 157 in trials for inflammatory bowel disease (PL-10, PLD-116, PL14736, Pliva, Croatia) heals ileoileal anastomosis in the rat. Surg Today. 2007;37(9):768-77.
14. Luján JJ, Németh ZH, Barratt-Stopper PA, Bustami R, Koshenkov VP, Rolandelli RH. Factors influencing the outcome of intestinal anastomosis. Am Surg. 2011;77(9):1169-75.
15. Lassen K, Revhaug A. Early oral nutrition after major upper gastrointestinal surgery: why not? Curr Opin

Clin Nutr Metab Care. 2006;9(5):613-7.
16. Oetzmann von Sochaczewski C, Lindner A, Heimann A, Balus A, Patel VH, Harrison MR, et al. Beyond magnamosis: a method to test sutureless esophageal anastomotic devices in living swine by creating an esophageal bypass loop for natural oral nutrition. J Laparoendosc Adv Surg Tech. 2019;29(6):852-5.
17. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. J Gastrointest Surg. 2009;13(3):569-75.
18. Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal operations. J Br Surg. 2005;92(6):673-80.
19. Silva TL, Maria de Lourdes S, Ferreira FR, Santos DC, Amatore C, Goulart MO. Quinone-based molecular electrochemistry and their contributions to medicinal chemistry: a look at the present and future. Curr Opin Electrochem. 2020;24:79-87.
20. Zaritzky M, Ben R, Johnston K. Magnetic gastrointestinal anastomosis in pediatric patients. J Pediatr Surg. 2014;49(7):1131-7.
21. Prilutsky V, Bakhir V. Electrochemically activated water: anomalous properties, mechanism of biological action. M, VNIIIMT. 1997.
22. Sung JJ, Tsoi KK, Ma TK, Yung M-Y, Lau JY, Chiu PW. Causes of mortality in patients with peptic ulcer bleeding: a prospective cohort study of 10,428 cases. Am J Gastroenterol. 2010;105(1):84-9.
23. Thantsha MS. Electrochemically activated water as an environmentally safe disinfectant: University of Pretoria; 2006.
24. You X-y, Chai L-y, Wang Y-y, Su Y-r, Na Z, Shu Y-d. Regeneration of activated carbon adsorbed EDTA by electrochemical method. rans. Nonferrous Met Soc China. 2013;23(3):855-60.
25. Lau JY, Yu Y, Tang RS, Chan HC, Yip H-C, Chan SM, et al. Timing of endoscopy for acute upper gastrointestinal bleeding. N Engl J Med. 2020;382(14):1299-308.
26. Duong V, Tarantola A, Ong S, Mey C, Choeung R, Ly S, et al. Laboratory diagnostics in dog-mediated rabies: an overview of performance and a proposed strategy for various settings. Int J Infect Dis. 2016;46:107-14.
27. Scott-Coombes D, Whawell S, Vipond M, Thompson J. Human intraperitoneal fibrinolytic response to elective surgery. J Br Surg. 1995;82(3):414-7.